Pharmacology of Antiepileptic Drugs

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Basic Mechanisms Underlying Seizures and Epilepsy

- **Seizure: the clinical manifestation of an abnormal and excessive excitation and synchronization of a population of cortical neurons**
- **Epilepsy: a tendency toward recurrent seizures unprovoked by any systemic or acute neurologic insults**
- **Epileptogenesis: sequence of events that converts a normal neuronal network into a hyperexcitable network**

Epidemiology of Seizures and Epilepsy

- **Seizures**
  - Incidence: approximately 80/100,000 per year
  - Lifetime prevalence: 9% (1/3 benign febrile convulsions)
- **Epilepsy**
  - Incidence: approximately 45/100,000 per year
  - 45-100 million people worldwide and 2-3 million in U.S.

Partial Seizures

localized onset can be determined

- **Simple**
- **Complex**
- **Secondary generalized**

Simple Partial Seizure

- Focal with minimal spread of abnormal discharge
- normal consciousness and awareness are maintained

Complex Partial Seizures

- Local onset, then spreads
- Impaired consciousness
- Clinical manifestations vary with site of origin and degree of spread
  - Presence and nature of aura
  - Automatisms
  - Other motor activity
- Temporal Lobe Epilepsy most common

Secondarily Generalized Seizures

- **Begins focally, with or without focal neurological symptoms**
- **Variable symmetry, intensity, and duration of tonic (stiffening) and clonic (jerking) phases**
- **Typical duration up to 1-2 minutes**
- **Postictal confusion, somnolence, with or without transient focal deficit**

Generalized seizures

- Absence seizures (Petit mal): sudden onset and abrupt cessation; duration less than 10 sec and rarely more than 45 sec; consciousness is altered; attack may be associated with mild clonic jerking of the eyelids or extremities, postural tone changes, autonomic phenomena and automatisms (difficult diff. diagnosis from partial); characteristic 2.5-3.5 Hz spike-and wave pattern

- Myoclonic seizures: myoclonic jerking is seen in a wide variety of seizures but when this is the major seizure type it is treated differently to some extent from partial leading to generalized

Generalized Seizures (cont)

- Atonic seizures: sudden loss of postural tone; most often in children but may be seen in adults

- Tonic-clonic seizures (grand mal): tonic rigidity of all extremities followed in 15-30 sec by tremor that is actually an interruption of the tonus by relaxation; relaxation proceeds to clonic phase with massive jerking of the body, this slows over 60-120 sec followed by stuporous state

Adult Seizure Types

- Complex partial seizures - 40%
- Simple partial seizures - 20%
- Primary generalized tonic-clonic seizures - 20%
- Absence seizures - 10%
- Other seizure types - 10%
- In a pediatric population, absence seizures occupy a greater proportion

How Does Epilepsy Develop?

- Acquired epilepsy
  - Physical insult to the brain leads to changes that cause seizures to develop—50% of patients with severe head injuries will develop a seizure disorder
  - Brain tumors, stroke, CNS infections, febrile seizures can all lead to development of epilepsy
  - Initial seizures cause anatomical events that lead to future vulnerability
  - Latent period occurs prior to development of epilepsy

How Does Epilepsy Develop?

- Genetic Epilepsies: Mutation causes increased excitability or brain abnormality
  - Cortical dysplasia—displacement of cortical tissue that disrupts normal circuitry
  - Benign familial neonatal convulsions